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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
PONNALURI, PADMASHRI	
ART UNIT	**PAPER NUMBER**
1639	

DATE MAILED: 07/27/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/836,865	LILIEN ET AL.	
	Examiner	Art Unit	
	Padmashri Ponnaluri	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 May 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,5,7-11,14,16,19-22 and 26-31 (in-part)* is/are pending in the application.

4a) Of the above claim(s) *13,15,17 and 18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,5,7-11,14,16,19-22 and 26-28* is/are rejected.

7)☒ Claim(s) *29-31* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *072204* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The amendment and response filed on 5/11/04 have been fully considered and entered into the application.

2. Claims 2-3, 6, 12 have been canceled by the amendment filed on 5/11/04.

3. Claims 23-25, 32-38 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 13.

4. Applicant's election without traverse of ' **PBDs of synaptotagmin SytI** as species of PBDs; **synaptotagmin SytIV** as target epitope; **10B encoding the 10B capsid protein** as gene encoding capsid protein; **1** as integer of n; **between 100 and 200 base pairs is the length** of the cDNA molecules, in Paper No. 15 is acknowledged.

5. Claims 13, 15, 17-18 (drawn to families of epitopes, NOTE SyntI is elected as target epitope), 27-29, claim 30 (b) and claim 31, withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species election, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 15.

6. The withdrawn claims 28-31 have been combined with examined claims in view of free of prior art of the elected species of 'target peptides', 'target epitopes' and 'length of cDNA molecules', as set forth in the office action mailed on 2/4/03.

7. The amended Claims 1, 14, 16 (in-part), withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species election, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in

Paper No 15. (NOTE that 'family of target peptides' (newly added) is drawn to non-elected invention).

8. Claims 1, 4-5, 7-11, 14, 16, 19-22, 26-31(in-part) (to the extent the elected 'target peptides as target epitopes', not to the family of target peptides as amended) are currently being examined in this application.

9. This application contains claims 1, 4-5, 7-11, 14, 16, 19-22, 26-27 (in-part) (drawn to family of target peptides or target epitopes) and claims 13, 15, 17-18 (drawn to families of epitopes, NOTE SyntI is elected as target epitope), drawn to an invention nonelected with traverse in the reply filed on 6/7/03. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Withdrawn Claim Rejections

10. The written description rejection of record has been withdrawn in view of the Amendments filed on 5/11/04.

11. The rejections of claims 1-12, 14, 16, 19-22 and 30 under 35 USC. 112, second paragraph set forth in the previous office action have been withdrawn in view of the amendment to the claims.

12. The rejection of claims 1-5, 8-12 under 35 USC. 102(b) as being anticipated by Houshmand et al has been withdrawn in view of the amendments to the claims.

New Claim Rejections Necessitated by the amendment

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

15. Claims 1, 4-5, 7-11, 14 and 16, 26-28 (in-part) are rejected under 35 U.S.C. 103(a) as being unpatentable over Houshmand et al (Analytical Biochemistry, 268, pages 363-370, March 1990) and Studier et al (US Patent 5,766,905).

Studier et al disclose display vectors comprising DNA encoding a portion of structural protein from cytoplasmic bacteriophage joined covalently to a protein of peptide of interest (refers to the PBD of the instant claims) (see the abstract). The reference teaches that the structural protein in the T7 capsid protein, and more specifically C-terminal residues of the capsid protein 10B (refers to the outersurface protein of the instant claims) joined to the N-terminal residue of the protein of interest (see the abstract). The reference teaches when a high

copy number display is desired, wild-type T7 capsid protein regulatory signals are employed (refers to instant claims 9-10), and when producing a larger fusion at a lower copy number on the assembled viral capsid lack wild-type capsid promoter and translation initiation signals (refers to instant claim 8) (i.e., see column 1). The reference teaches that the display vectors of the present invention can be used to screen or select virus bearing a capsid fusion proteins, and expression screening of DNA library in an effort to identify a protein having particular binding characteristics. The reference teaches randomly generated DNA fragments of interest (e.g., fragments from a cDNA library) are cloned into the virus-based display vector to a produce a library (refers to the cDNA library of the instant claims) (e.g., see column 4). The reference teaches that the a common laboratory technique for phage screening is to plate packaged phage on a lawn of host cells at an appropriate phage dilution to produce a suitable number of plaques per plate to facilitate efficient screening (refers to the instant claim 11)(i.e., see column 4). The reference teaches that the virus from the plaques can be transformed to nitrocellulose membrane and screened using affinity reagent (or target). The reference teaches that from the plaques identified as the source of the viral particles displaying the protein or peptide of interest on its surface DNA is isolated that encodes the protein, and the DNA is further characterized to determine the sequence (i.e., see column 5).

The claimed invention differs from the prior art teachings by reciting that the phage display library is screened against an array of predetermined target peptides.

Houshmand et al disclose a heptapeptide library displayed by bacteriophage T7 (refers to instant claim step (a) (i.e., see the abstract). Epitopes of monoclonal antibodies F4, F5 and LT1 were adsorbed to the wells of microtiter plate (refers to the array of epitopes of the instant

claims) and virus (phage library) were adsorbed to the wells (previously coated with the Mabs) of the microtiter plate (refers to step (b) of the instant claims). Phage particles adsorbed to the coated surface were eluted by SDS, and the eluted phage were amplified in E.coli (refers to steps d) and e) of the instant claims and instant claim 11) (i.e., see right column in page 4, under panning procedure). The selection was repeated four times (refers to instant claims 4-5). After final panning the phage was cloned by plaque isolation. For analysis of expressed peptide sequences, a segment of the phage DNA was amplified by PCR . The nucleotide sequences of the DNA products were then determined ((refers to step e) of the instant claims). The reference discloses the fusion polypeptide is present in 415 copies on each phage particles (refers to instant claims 8-9).

Thus, it would have been obvious to a person skilled in the art at the time the invention was made to use capsid protein 10B of T7 phage to fuse with a peptide of interest in the method of screening DNA library for identifying a protein or peptide having particular binding characteristics taught by Studier et al in the method of screening the phage display library against an array of target peptides taught by Houshmand et al. A person skilled in the art would have been motivated to use the 10B capsid protein of T7 phage to fuse the peptide of interest such that the fusion protein is displayed in larger number (higher copy number), and screen the display library against an array of targets such that multiple different epitopes are characterized in one single assay.

16. Claims 1, 4-5, 7-11, 14, 16, 19-22, 26-28 (in-part) are rejected under 35 U.S.C. 103(a) as being unpatentable over Studier et al (US Patent 5,766,905), Houshmand et al and Geysen (US Patent 4,833,092).

Studier et al and Houshmand et al have been discussed supra. The claimed invention further differs from the prior art teachings by reciting that the target epitopes (target peptides) are synthesized in parallel on polyethylene pins (the instant claim 14). Houshmand et al and Studier et al teach different methods of preparing phage display libraries and methods of screening the phage display library using multiple targets arranged in array format. Houshmand et al and Studier et al do not teach the target epitopes are arranged or synthesized on polyethylene pins. However, it is well known in the combinatorial solid phase synthesis technology to use Multipins compatible with standard microplate arrays of 96 wells. Geysen teaches methods of synthesis of peptides on polyethylene pins. The instant specification refers to the well known prior art, for example in page 8 last paragraph through page 9 discloses that '...simultaneous synthesis of numerous individual peptides of known sequence on a solid support array, such as on "Multipins" that are arrayed in a manner complementary to the wells of standard 96-well microplates. This is preferably done using the MULTIPIN peptide synthesis kit from Chiron by similar methods such as those described in US Patent 5,266,684....'. The instant claimed method uses the well known Mutipin method disclosed by Geysen in synthesis of the target peptides. Thus it would have been obvious to one skilled in the art at the time the invention was made to use the well known and commercially available Multipin technology in synthesizing the target peptides on multipins which are compatible with 96-well microtitre plate, such that the Pins of the Multipin fits into the 96 well microtiter plate containing phage display library. Thus, it would have been obvious to one skilled in the art to use the peptides attached to the pins (array of peptides) in the method of screening the phage display library taught by Houshmand et al and Studier et al.

And further the methods of synthesis of the target peptides does not limit the patentability of the claimed method of screening, since the array of peptides (products) are used in the claimed method. The methods of synthesis of the peptides on the multipins is considered as product-by-process. The instant claim array of peptides is written as product-by-process claims. "Eventhough the product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability is based on the product itself. The patentability of a product does hot depend on its method of production. If the product in the product-by-process claims is same or as obvious from the product of the prior art, the claim is unpatentable even though the prior art product was made by a different process." In re Thorpe, 777 F. 2d 695, 698, 227 U. S. P. Q. 964, 966 (Fed. Cir. 1985). (see MPEP 2113).

Allowable Subject Matter

17. Claims 29-31 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Response to Arguments

18. Applicant's arguments filed on 5/11/04, regarding the rejection of claims over Houshmand et al and Studier et al; and the rejections over Houshmand et al, Studier et al and Geysen have been fully considered but they are not persuasive.

The rejections over Houshmand et al and Studier et al have been rewritten to address all the limitations of the instantly amended claim limitations and amended claim dependency. However, applicants' traversal of the rejection has been considered and are not found persuasive for the following reasons.

Applicants argue the references individually, and in response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicants' arguments or assertions that none of the art at the time the invention was made to use cDNA library as a phage display library in the T7 system. Applicants arguments and assertions are not persuasive, because it is well known in the art at the time the invention was filed to display cDNA in T7 system, i.e., see the cited art Studier et al and Houshmand et al. Applicants further argue that the importance of the claimed method (preselected peptide binding to epitope family represented in the array of claim 1(b)). Applicant's arguments have been considered and are not persuasive since that particular limitation was withdrawn as drawn to non-elected invention. Thus, for the reasons set forth above the combined teachings of Studier et al and Houshmand et al is obvious over the claimed invention. And applicants' does not really traverse the teachings of Geysen or the use of the Mutipin technology in the claimed array of peptide synthesis. Thus, it would have been obvious to one skilled in the art to make and screen the phage display libraries against the array of peptides from the combined teachings of Houshmand et al, Studier et al and Geysen.

Conclusion

19. No claims are allowed.

20. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Padmashri Ponnaluri whose telephone number is 571-272-0809. The examiner is on Increased Flex Schedule and can normally be reached on Monday through Friday between 7 AM and 3.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

PADMASHRI PONNALURI
PRIMARY EXAMINER

Padmashri Ponnaluri
Primary Examiner
Art Unit 1639

22 July 2004